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NEWS	2	Dec 17	The CA Lexicon available in the CAPLUS and CA files
NEWS	3	Feb 06	Engineering Information Encompass files have new names
NEWS	4	Feb 16	TOXLINE no longer being updated
NEWS	5	Apr 23	Search Derwent WPINDEX by chemical structure
NEWS	6	Apr 23	PRE-1967 REFERENCES NOW SEARCHABLE IN CAPLUS AND CA
NEWS	7	May 07	DGENE Reload
NEWS	8	Jun 20	Published patent applications (A1) are now in USPATFULL
NEWS	9	JUL 13	New SDI alert frequency now available in Derwent's DWPI and DPCI
NEWS	10	Aug 23	In-process records and more frequent updates now in MEDLINE
NEWS	11	Aug 23	PAGE IMAGES FOR 1947-1966 RECORDS IN CAPLUS AND CA
NEWS	12	Aug 23	Adis Newsletters (ADISNEWS) now available on STN
NEWS	13	Sep 17	IMSworld Pharmaceutical Company Directory name change to PHARMASEARCH
NEWS	14	Oct 09	Korean abstracts now included in Derwent World Patents Index
NEWS	15	Oct 09	Number of Derwent World Patents Index updates increased
NEWS	16	Oct 15	Calculated properties now in the REGISTRY/ZREGISTRY File
NEWS	17	Oct 22	Over 1 million reactions added to CASREACT
NEWS	18	Oct 22	DGENE GETSIM has been improved
NEWS	19	Oct 29	AAASD no longer available
NEWS	20	Nov 19	New Search Capabilities USPATFULL and USPAT2
NEWS	21	Nov 19	TOXCENTER(SM) - new toxicology file now available on STN
NEWS	22	Nov 29	COPPERLIT now available on STN
NEWS	23	Nov 29	DWPI revisions to NTIS and US Provisional Numbers
NEWS	24	Nov 30	Files VETU and VETB to have open access
NEWS	25	Dec 10	WPINDEX/WPIDS/WPIX New and Revised Manual Codes for 2002
NEWS	26	Dec 10	DGENE BLAST Homology Search
NEWS EXPRESS			August 15 CURRENT WINDOWS VERSION IS V6.0c, CURRENT MACINTOSH VERSION IS V6.0 (ENG) AND V6.0J (JP), AND CURRENT DISCOVER FILE IS DATED 07 AUGUST 2001
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FILE 'HOME' ENTERED AT 12:06:26 ON 13 DEC 2001

=> file embase medline caplus embase uspatfull  
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FILE 'USPATFULL' ENTERED AT 12:06:52 ON 13 DEC 2001

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=> s fenofibrate

L1 2786 FENOFIBRATE

=> s soybean oil and coconut oil or canola oil or corn oil or palm oil or  
cottonseed oil or olive oil or peanut oil or safflower oil or sesame oil

L2 94973 SOYBEAN OIL AND COCONUT OIL OR CANOLA OIL OR CORN OIL OR PALM  
OIL OR COTTONSEED OIL OR OLIVE OIL OR PEANUT OIL OR SAFFLOWER  
OIL OR SESAME OIL

=> s emulsifier or emulsion or sorbitan fatty acid or castor oil or ethoxylate

L3 419779 EMULSIFIER OR EMULSION OR SORBITAN FATTY ACID OR CASTOR OIL OR  
ETHOXYLATE

=> s l1 and l2 and l3

L4 67 L1 AND L2 AND L3

=> s l4 and py<1999

1 FILES SEARCHED...

3 FILES SEARCHED...

L5 6 L4 AND PY<1999

=> dup rem l5

PROCESSING COMPLETED FOR L5

L6 6 DUP REM L5 (0 DUPLICATES REMOVED)

=> d l6 1-6 ab bib kwic

L6 ANSWER 1 OF 6 USPATFULL

AB A method for preventing or treating high serum levels of cholesterol  
and

lipids in a mammal, said method comprising orally administering an  
effective amount of natural lycopene to prevent or treat high serum  
levels of cholesterol or lipids to a mammal in need of such treatment.  
Also disclosed is an oral pharmaceutical composition in unit dosage  
form

for oral administration for the prevention or treatment of high serum

levels of cholesterol and/or lipids in a mammal, said composition comprising an effective amount of natural lycopene to prevent or treat high serum levels of cholesterol or lipids in a mammal and in a sufficient amount to achieve a level of serum cholesterol of less than 200 mg per deciliter over the course of treatment, and a pharmaceutically acceptable carrier therefor.

AN 2001:112374 USPATFULL

TI Methods of preventing and/or treating high serum levels of cholesterol and/or lipids

IN Clark, James P., Naperville, IL, United States  
Dunker, Manfred S., Palos Park, IL, United States

PA Henkel Corporation, Gulph Mills, PA, United States (U.S. corporation)

PI US 6262109 B1 20010717  
WO 9619217 19960627 <--

AI US 1997-849977 19970822 (8)  
WO 1995-US16774 19951222  
19970822 PCT 371 date  
19970822 PCT 102(e) date

DT Utility

FS GRANTED

EXNAM Primary Examiner: Criares, Theodore J.

LREP Drach, John E., Murphy, Glenn J., Ettelman, Aaron R.

CLMN Number of Claims: 7

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 330

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PI US 6262109 B1 20010717  
WO 9619217 19960627 <--

SUMM The drugs which are being used in these studies are, for example, clofibrate, gemfibrozil, **fenofibrate** and bezafibrate or a combination of cholestyramine and niacin. These reports clearly support the theory that lowering of serum cholesterol. . .

SUMM . . . natural tocopherol, especially alpha-tocopherol, with or without natural beta-carotene. The natural beta-carotene is preferably obtained from natural sources, such as **palm oil** or algae.

SUMM . . . natural tocopherols are derived from vegetable oils. Soy oil is the most widely used source. Sunflower, corn, peanut, rapeseed and **cottonseed oils** may also be used. Natural tocotrienol and natural tocopherols are very different from that produced by chemical synthesis, i.e., synthetic. . .

SUMM . . . carrier. Thus, for example, when administered orally, the active ingredient is formulated in the form of soft gelatin capsule, elixir, **emulsion** and the like employing methods well known in the art. Suitable formulations and formulation techniques can be found in Remington's. . .

DETD About 5 mg units of lycopene is mixed in a suitable blender with about 450 mg of **peanut oil**. It is then dispensed in the form of soft gelatin capsule.

L6 ANSWER 2 OF 6 USPATFULL

AB The present invention relates to novel tocotrienols and tocotrienol-like compounds displaying biological activity. The tocotrienols and tocotrienol-like compounds of this invention may be conveniently obtained from biological sources or by chemical synthesis and may be used in pharmaceutical compositions, foodstuffs and dietary supplements.

This invention also relates to the use of tocotrienols, tocotrienol-like compounds, and mixtures thereof, as hypocholesterolemic, antithrombotic, antioxidizing, antiatherogenic, antiinflammatory and immunoregulatory agents, or as agents useful to decrease lipoprotein (a) concentration in

the blood or to increase feed conversion efficiency.

AN 1998:124588 USPATFULL  
TI Tocotrienols and tocotrienol-like compounds and methods for their use  
IN Lane, Ronald H., Phoenix, AZ, United States  
Qureshi, Asaf A., Madison, WI, United States  
Salser, Winston A., Pacific Palisades, CA, United States  
PA LipoGenics, Inc., Scottsdale, AZ, United States (U.S. corporation)  
PI US 5821264 19981013 <--  
AI US 1996-719284 19960924 (8)  
RLI Continuation of Ser. No. US 1994-244215, filed on 15 Aug 1994, now patented, Pat. No. US 5591772 which is a continuation-in-part of Ser. No. US 1991-796486, filed on 22 Nov 1991, now abandoned  
DT Utility  
FS Granted  
EXNAM Primary Examiner: Raymond, Richard L.  
LREP Lyon & Lyon LLP  
CLMN Number of Claims: 32  
ECL Exemplary Claim: 1  
DRWN 14 Drawing Figure(s); 13 Drawing Page(s)  
LN.CNT 3191

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PI US 5821264 19981013 <--  
SUMM . . . ("T"). Tocotrienols and tocopherols occur naturally in small quantities in a wide variety of plant sources, such as rice bran, **palm oil** and barley (A. A. Qureshi et al., "Lowering of Serum Cholesterol in Hypercholesterolemic Humans by Tocotrienols (Palmvitee)", Am. J. Clin. . . .

SUMM . . . al. (1986), supra. Various human and animal studies have confirmed the impact of pure tocotrienols, isolated from barley, oats and **palm oil**, on cholesterol biosynthesis, specifically LDL-cholesterol (A. A. Qureshi et al., "Dietary Tocotrienols Reduce Concentrations of Plasma Cholesterol,

Apolipoprotein B, Thromboxane. . . By Tocotrienols (Palmvitee)", Am. J. Clin.

Nutr., 53, pp. 1021S-26S (1991); D. T. S. Tan et al., "The Effect Of **Palm Oil** Vitamin E Concentrate On The Serum And Lipoprotein Lipids In Humans", Am. J. Clin. Nutr., 53, pp. 1027S-30S (1991)). In. . .

DETD TRF Standard--A tocotrienol-rich fraction (TRF) obtained from **palm oil** (A. A. Qureshi et al. (1991), supra). The TRF Standard contains varying amounts of .alpha.-, .gamma.- and .delta.-tocotrienol and .alpha.-tocopherol. . . .

DETD . . . milkweed, flax, sesame, rice bran, parboiled brown rice, brown rice flour, olives, vegetable oil distillant, fruit concentrate evaporate, barley bran, **palm oil**, wheat germ oil, rice bran oil, barley oil, **coconut oil**, **cottonseed oil**, **soybean oil**, other

cereal grains and other cereal grain oils, plant tissues, flowers, bushes (such as juniper), trees (such as pine and. . . .

DETD Pharmaceutical compositions may take the form of tablets, capsules, **emulsions**, suspensions and powders for oral administration, sterile solutions or **emulsions** for parenteral administration,

sterile solutions for intravenous administration and gels, lotions and cremes for topical application. The pharmaceutical compositions may. .

DETD . . . thereof, and a pharmaceutically acceptable carrier. Such carriers may be solid or liquid, such as, for example, cornstarch, lactose, sucrose, **olive oil** or **sesame oil**. If a solid carrier is used, the dosage forms may be tablets, capsules or lozenges. Liquid dosage forms include soft. . .

DETD . . . used in combination with bile acid sequestrants, such as Cholestyramine and Colestipol; fibric acid derivatives, such as, Clofibrate, Gemfibrozil, Bezafibrate, **Fenofibrate**, and Ciprofibrate; HMGCoA inhibitors, such as Lovastatin, Mevastatin, Pravastatin, Simvastatin and SRI-62320; Probucol; Nicotinic Acid; its derivatives and conjugates, such. . .

DETD

Ingredients	Weight (g)
-------------	------------

Corn (8.8% protein)	615.0
Soybean Meal	335.0
<b>Corn Oil</b>	10.0
Calcium Carbonate	10.0
Dicalcium Phosphate	20.0
Iodized Salt	5.0
Mineral Mixture <sup>sup.a</sup>	2.5
Vitamin Mixture <sup>sup.b</sup>	2.5

<sup>sup.a</sup> Mineral mixture contained per kg feed: zinc sulfate.H<sub>sub</sub>.2. . .

DETD . . . of the chicken mash diet containing a 5% supplement of various oils. The control diet included a supplement of 5% **corn oil**. After 4 weeks, the birds were fasted for 36 hours and then refed for 48 hours prior to sacrifice (at. . .

DETD . . . Glucose

1)

Chick Diet + 5.0%	185.1 $\pm$ 5.1 <sup>sup.A</sup>
	110.3 $\pm$ 4.95 <sup>sup.A</sup>
	61.9 $\pm$ 4.49 <sup>sup.A</sup>
	90.2 $\pm$ 2.17 <sup>sup.A</sup>
	124.6 $\pm$ 2.30 <sup>sup.A</sup>
<b>Corn Oil</b> (CDC)	(100.0) <sup>sup.2</sup>
	(100.0) <sup>sup.2</sup>
	(100.0) <sup>sup.2</sup>
	(100.0) <sup>sup.2</sup>
	(100.0) <sup>sup.2</sup>

2)

Chick Diet + 5.0%	129.7 $\pm$ 4.1 <sup>sup.B</sup>
	99.8 $\pm$ 3.57 <sup>sup.A</sup>
	27.9 $\pm$ 2.60 <sup>sup.B</sup>
	84.5 . . .

DETD . . . (nmoles/mg/min)<sup>sup.3</sup>

1)  
 Chick Diet + 5.0%  
     185.1  $\pm$  4.12.sup.A  
         110.3  $\pm$  4.95.sup.A  
             61.9  $\pm$  1.49.sup.A  
                 344.3  $\pm$  1.49.sup.A  
                     0.855  $\pm$  0.084.sup.A  
  
**Corn Oil** (CDCO)  
     (100.0).sup.4  
         (100.0).sup.4  
             (100.0).sup.4  
                 (100.0).sup.4  
                     (100.0).sup.4

2)  
 Chick Diet + 5.0%  
     184.7  $\pm$  6.50.sup.A  
         109.6  $\pm$  2.83.sup.A  
             61.7  $\pm$  1.71.sup.A  
                 339.3  $\pm$  19.7.sup.A  
                     0.837  $\pm$  0.081.sup.A  
  
**Corn Oil** + Waxes;  
     (99.8) (99.4) (99.7)  
                     (98.5) (97.9)

50 ppm  
 3)  
 Chick Diet + 5.0%  
     173.8  $\pm$  7.31.sup.A  
         106.2  $\pm$  4.69.sup.A  
             58.1  $\pm$  1.77.sup.A  
                 317.1  $\pm$  14.4.sup.A,B  
                     0.846  $\pm$  0.072.sup.A  
  
**Corn Oil** + Waxes;  
     (93.9) (96.3) (93.9)  
                     (92.1) (98.9)

5,000 ppm  
 4)  
 Chick Diet + 5.0%  
     165.9  $\pm$  4.90.sup.B  
         108.5  $\pm$  4.68.sup.A  
             57.9  $\pm$  1.48.sup.A  
                 304.5  $\pm$  14.4.sup.B  
                     0.902  $\pm$  0.080.sup.A  
  
**Corn Oil** + Waxes;  
     (89.6) (98.4) (93.5)  
                     (88.4) (105.5)

10,000 ppm  
 5)  
 Chick Diet + 5.0%  
     134.8  $\pm$  3.82.sup.C  
         104.3  $\pm$  3.99.sup.A  
             25.9  $\pm$  1.02.sup.B  
                 276.0  $\pm$  17.4.sup.C  
                     1.068  $\pm$  0.047.sup.B  
  
**Corn Oil** +  
     (72.8) (94.6) (41.8)  
                     (80.2) (124.9)

Tocotrienol-Rich-  
 Fraction; 50 ppm

6)  
 Chick Diet + 5.0%

180.2  $\pm$  6.01.sup.A  
104.0  $\pm$  4.57.sup.A

DETD

(ng/ml)

1)

Chick Diet + 5.0%

61.4  $\pm$  2.4.sup.A  
90.2  $\pm$  1.17.sup.A  
124.6  $\pm$  2.3.sup.A  
16.7  $\pm$  1.69.sup.A  
7.2  $\pm$  0.48.sup.A

Corn Oil (CDCO)

(100.0).sup.3  
(100.0).sup.3  
(100.0).sup.3  
(100.0).sup.3  
(100.0).sup.3

2)

Chick Diet + 5.0%

62.5  $\pm$  1.9.sup.A  
91.5  $\pm$  1.48.sup.A  
126.7  $\pm$  2.1.sup.A  
15.8  $\pm$  1.29.sup.A  
7.5  $\pm$  0.42.sup.A

Corn Oil + Waxes;

(102.0).sup.3  
(101.4).sup.3  
(101.7).sup.3  
(94.6).sup.3  
(104.2).sup.3

50 ppm

3)

Chick Diet + 5.0%

63.6  $\pm$  2.8.sup.B  
95.2  $\pm$  1.01.sup.A  
123.9  $\pm$  1.52.sup.A  
16.4  $\pm$  1.66.sup.A  
7.4  $\pm$  0.36.sup.A

Corn oil + Waxes;

(103.8).sup.3  
(105.5).sup.3  
(99.4).sup.3  
(98.2).sup.3  
(102.8).sup.3

5,000 ppm

4)

Chick Diet + 5.0%;

60.4  $\pm$  1.9.sup.A  
96.1  $\pm$  1.90.sup.A  
124.3  $\pm$  1.18.sup.A  
16.8  $\pm$  1.67.sup.A  
7.4  $\pm$  0.87.sup.A

Corn oil + Waxes;

(98.5).sup.3  
(106.5).sup.3  
(99.8).sup.3  
(100.6).sup.3  
(102.8).sup.3

10,000 ppm

5)

Chick Diet + 5.0%

68.5  $\pm$  2.1.sup.B

73.2  $\pm$  1.69.sup.B

86.4  $\pm$  1.55.sup.B

12.4  $\pm$  1.42.sup.B

5.7  $\pm$  0.64.sup.B

Corn oil +

(111.7).sup.3

(81.2).sup.3

(69.3).sup.3

(74.3).sup.3

(79.2).sup.3

Tocotrienol-Rich-

Fraction; 50 ppm

6)

Chick Diet + 5.0%

65.8  $\pm$  1.2.sup.B

89.5  $\pm$  1.21.sup.A

L6 ANSWER 3 OF 6 USPATFULL

AB Ergostanone derivatives substituted with dissaccharides are cholesterol absorption inhibitors useful in the treatment of hypercholesterolemia and related disorders. These cholesterol absorption inhibitors may be employed alone or in combination with other cholesterol lowering

agents.

AN 97:118019 USPATFULL

TI Steroidal glycosides as antihyperlipidemic agents

IN Kim, Dooseop, Westfield, NJ, United States

PA Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)

PI US 5698527 19971216 <--

AI US 1996-688582 19960730 (8)

DT Utility

FS Granted

EXNAM Primary Examiner: Owens, Amelia

LREP Quagliato, Carol S, Winokur, Melvin

CLMN Number of Claims: 13

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1307

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PI US 5698527 19971216 <--

SUMM . . . lipid deposition in the rabbit aorta. Male New Zealand white rabbits are fed a diet containing 0.4% cholesterol and 5% **peanut oil** for 1 week (meal-fed once a day). After 1 week, the rabbits are dosed daily with the desired concentration of. . .

SUMM . . . forms as tablets, capsules (each including timed release and sustained release formulations), pills, powders, granules, elixirs, tinctures, suspensions, syrups and **emulsions**. Likewise, they may also be administered in intravenous (both bolus and infusion), intraperitoneal, subcutaneous or intramuscular form, all using forms.

SUMM . . . synthetase inhibitors (also known as squalene synthase inhibitors), acylcoenzyme A: cholesterol acyltransferase (ACAT) inhibitors; probucol; niacin; fibrates such as clofibrate, **fenofibrate**, and gemfibrozil; bile acid sequestrants; LDL (low density lipoprotein) receptor inducers; vitamin B.sub.6 (also known as pyridoxine) and the pharmaceutically. . .



SUMM . . . 1000 mg probucol, up to 2 g clofibrate, 0.5 to 8 g of niacin, 800 to 1500 mg gemfibrozil or **fenofibrate**, or 20 to 300 mg of an LDL receptor gene inducer.

L6 ANSWER 4 OF 6 USPATFULL

AB Therapeutic compositions comprising an effective amount of at least one carbonyl trapping agent alone or in combination with a therapeutically effective of a co-agent or medicament are disclosed. The compositions are used to treat a mammal suffering from a neurological disease characterized by covalent bond crosslinking between the nerve cells, other cellular structures and their intracellular and extracellular components, with disease induced carbonyl-containing aliphatic or aromatic hydrocarbons present in mammals.

AN 97:83944 USPATFULL

TI Methods of treating neurological diseases and etiologically related symptomology using carbonyl trapping agents in combination with previously known medicaments

IN Shapiro, Howard K., 214 Price Ave. F32, Narberth, PA, United States 19072

PI US 5668117 19970916 <--

AI US 1993-62201 19930629 (8)

RLI Continuation-in-part of Ser. No. US 1993-26617, filed on 23 Feb 1993, now abandoned which is a continuation of Ser. No. US 1991-660561, filed on 22 Feb 1991, now abandoned

DT Utility

FS Granted

EXNAM Primary Examiner: Kight, John; Assistant Examiner: Leary, Louise

LREP Perrella, D. J.

CLMN Number of Claims: 29

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 3963

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PI US 5668117 19970916 <--

SUMM . . . Grundy, 1990), bezafibrate (Olsson and Lang, 1978a; Olsson and Lang, 1978b; Zimmermann and coworkers, 1978; Monk and Todd, 1987) and **fenofibrate** (Elsom and coworkers, 1976; Wulfert and coworkers, 1976); metformin (Hermann, 1979); guar gum (Lalor and coworkers, 1990); 3-hydroxy-3-methylglutaryl-CoA reductase inhibitors. . .

SUMM . . . for patients suffering from these chronic, age-related diseases. Previously recognized drugs for treatment of atherosclerosis include hypolipidemic agents such as **fenofibrate** (Elsom and coworkers, 1976; Wulfert and coworkers, 1976), bezafibrate (Olsson and Lang, 1978a; Olsson and Lang, 1978b; Zimmermann and coworkers, . . .

SUMM . . . acetate, generating primary amine groups still covalently

bound

to the polysaccharide. Chitosan has recognized uses in water treatment, in photographic **emulsions**, and in improving the dyability of synthetic fabrics and fibers. The free amine groups in this substance also give it. . .

SUMM The ingredients as listed on the label are: "dicalcium phosphate, d-calcium pantothenate, pyridoxine hydrochloride, hydrogenated **cottonseed oil**, cellulose, niacinamide, rifoflavin, thiamine mono-nitrtate, stearic acid, modified cellulose gum, magnesium stearate, silica, resin, gum acacia, hydroxypropylcellulose, rice bran, yeast, . . .

DETD **fenofibrate**, dosage range from 40 mg daily to 500 mg daily;

DETD **fenofibrate**, dosage range from 40 mg daily to 500 mg daily;

L6 ANSWER 5 OF 6 USPATFULL

AB There is provided a carrier for hydrophobic drugs, and pharmaceutical compositions based thereon, which carrier comprises a digestible oil and

a pharmaceutically acceptable surfactant component for dispersing the oil in vivo upon administration of the carrier, which comprises a hydrophilic surfactant, said surfactant component being such as not to substantially inhibit the in vivo lipolysis of the digestible oil.

AN 97:58921 USPATFULL

TI Delivery systems for hydrophobic drugs

IN Lacy, Jonathan Ernest, Swindon, United Kingdom  
Embleton, Jonathan Kenneth, Berkshire, United Kingdom

PA R. P. Scherer Corporation, Troy, MI, United States (U.S. corporation)

PI US 5645856 19970708 <--  
WO 9524893 19950921 <--

AI US 1995-446874 19950606 (8)  
WO 1995-GB561 19950316  
19950606 PCT 371 date  
19950606 PCT 102(e) date

PRAI GB 1994-5304 19940316

DT Utility

FS Granted

EXNAM Primary Examiner: Page, Thurman K.; Assistant Examiner: Spear, James M.

LREP Pearne, Gordon, McCoy & Granger LLP

CLMN Number of Claims: 23

ECL Exemplary Claim: 1

DRWN 3 Drawing Figure(s); 3 Drawing Page(s)

LN.CNT 1382

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PI US 5645856 19970708 <--  
WO 9524893 19950921 <--

SUMM . . . include a surfactant component. Lipophilic surfactants (i.e. HLB<10) are capable of promoting some emulsification of the oil but the resulting **emulsions** are normally too crude, in terms of size, to be useful. Hydrophilic surfactants (i.e. HLB>10) are much superior with respect to forming oil-in-water (o/w) **emulsions** and can be used to produce fine, uniform **emulsions** which are more likely to empty rapidly and uniformly from the stomach and coupled with a very large surface area. . . .

DRWD 6. **Castor oil ethoxylates** (low **ethoxylate** content, HLB<10) e.g. \_\_\_\_\_  
Etocas 5 (5 moles of ethylene oxide reacted with 1 mole of **castor oil**) Sandoxylate 5 (5 moles of ethylene oxide reacted with 1 mole of **castor oil**)

DRWD 7. Acid and ester **ethoxylates**--formed by reacting ethylene oxide with fatty acids or glycerol esters of fatty acids (HLB<10) e.g. \_\_\_\_\_ Crodet 04  
(polyoxyethylene (4) lauric acid) Cithrol. . . .

DRWD . . . of natural or hydrogenated vegetable oil triglyceride and a polyalkylene polyol (HLB<10)

e.g. \_\_\_\_\_ L  
abrafil M1944CS (polyoxyethylated apricot kernal oil) Labrafil M2125CS (polyoxyethylated **corn oil**) Gelucire 37/06 (polyoxyethylated hydrogenated oil)

DRWD 2. Polyoxyethylene **sorbitan fatty acid** derivatives e.g. \_\_\_\_\_ Tween 20  
(polyoxyethylene (20) monolaureate) Tween 80 (polyoxyethylene (20) monooleate) Criliet 4 (polyoxyethylene (20) monooleate) Montanox 40 (polyoxyethylene (20) monopalmitate)

DRWD 3. **Castor oil** or hydrogenated castor oil  
**ethoxylates** (HLB>10) e.g. \_\_\_\_\_ C  
 remophor EL (polyoxyethylene (35) **castor oil**  
 )Cremophor RH40 (polyoxyethylene (40) hydrogenated  
**castor oil**)Etocas 40 (polyoxyethylene (40)  
**castor oil**)Nikkol HCO-60 (polyoxyethylene (60)  
 hydrogenated **castor oil**  
 )

DRWD 4. Fatty acid **ethoxylates** (HLB>10)  
 e.g. \_\_\_\_\_ Myrj 45

(polyoxyethylene  
 (8) stearate)Tagat L (polyoxyethylene (30) monolaurate)Marlosol  
 1820 (polyoxyethylene (20) stearate)Marlosol OL15 (polyoxyethylene (15)  
 oleate)

DRWD 5. Alcohol **ethoxylates** (HLB>10) e.g. \_\_\_\_\_  
 Brij 96 (polyoxyethylene (10) oleyl ether)Volpo 015  
 (polyoxyethylene (15) oleyl ether)Marlowet OA30 (polyoxyethylene (30)  
 oleyl ether)Marlowet LMA20 (polyoxyethylene (20)). . .

DRWD . . . oils which may be used include those containing saturated  
 C.sub.6 -C.sub.12 fatty acids, for instance fractionated vegetable oils  
 e.g. fractionated **coconut oils**. Specific examples of  
 useful capric and/or caprylic triglyceride oils include: Miglyol 810,  
 Miglyol 812, Neobee M5, Neobee 0, Captex 300,. . .

DRWD Lipid regulating agents: bezafibrate, clofibrate, **fenofibrate**,  
 gemfibrozil, probucol.

DRWD In the stomach the oil is physically emulsified with gastric juice to  
 form an oil-in-water (o/w) **emulsion**. Hydrophobic drugs will  
 reside predominantly within the dispersed (i.e. oil) phase of this  
**emulsion** as either a solution or partial suspension.

DRWD The o/w **emulsion** is not digested to any significant extent in  
 the stomach with the result that the hydrophobic drug will enter the.

DRWD . . . much higher solubilising power for hydrophobic drugs than pure  
 bile salt micelles. This is illustrated with the hydrophobic  
 antihyperlipoproteinemic drug **fenofibrate** which we have shown  
 is >20 times more soluble in mixed micelles than simple bile salt  
 micelles.

DETD Effects of a Hydrophilic Surfactant on the Lipolysis Rate for  
 Fractionated **Coconut Oil** (FCO) in the absence of a  
 Lipophilic Surfactant

DETD The drugs investigated using this method were: Carbamazepine,  
 griseofulvin, **fenofibrate** and probucol.

DETD

Solubility (Relative to Buffer)

Experiment

Carbamazepine

Griseofulvin

**Fenofibrate**

Probucol

i	1	1	1	1*
ii	1.1	4.6	38.5	>71.0
iii	2.6	7.4	188.5	>320.0
iv	2.7	6.6	930.0	>77.0

\*Buffer solubility of. . .

DETD

Component mg/cap % w/w

Fractionated <b>coconut oil</b>		
	190	17.19
Imwitor 988	285	25.79
Cremophor RH40	285	25.79
Maisine 35-1	95	8.60
Ethanol	200	18.10
Progesterone	50	4.52
TOTAL	1105	100

---

DETD

Polysorbate 80	
275 mg	
Priolene 275 mg	
<b>Soybean Oil</b>	
185 mg	
Triacetin	
185 mg	
<b>Fenofibrate</b>	
80 mg	

---

DETD

Cremophor RH40	300 mg
Fractionated <b>Coconut Oil</b>	
240 mg	
Maisine	200 mg
Imwitor 988	110 mg
Ethanol	100 mg
Progesterone	50 mg

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DETD

Cremophor RH40	225 mg
Fractionated <b>Coconut Oil</b>	
315 mg	
Crill 1	360 mg
Griseofulvin	100 mg

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DETD

Polysorbate 80	
280 mg	
<b>Soybean Oil</b>	
340 mg	
Priolene 280 mg	
Probucol 100 mg	

---

DETD

Labrasol	330 mg
Fractionated <b>Coconut Oil</b>	
120 mg	
Phenytoin	50 mg

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DETD

Component	Concentration (% w/w)
-----------	-----------------------

Progesterone	4
Fractionated <b>coconut oil</b>	
16	
Cremophor RH40	28
Lauroglycol	37
Ethanol	15

DETD  
Component      Concentration (% w/w)

Progesterone 4  
Soybean oil 16  
Tween 80 20  
Imwitor 988 45  
Ethanol 15

CLM      What is claimed is:  
5. A pharmaceutical composition according to claims 2, 3 or 4 wherein said hydrophilic surfactant component comprises a **castor oil** or hydrogenated castor **ethoxylate** having an HLB value greater than 10.  
  
6. A pharmaceutical composition according to claim 5, wherein said hydrophilic surfactant component comprises a polyoxyethylene hydrogenated **castor oil**.

L6      ANSWER 6 OF 6      USPATFULL

AB      The present invention relates to novel tocotrienols and tocotrienol-like compounds displaying biological activity. The tocotrienols and tocotrienol-like compounds of this invention may be conveniently obtained from biological sources or by chemical synthesis and may be used in pharmaceutical compositions, foodstuffs and dietary supplements.  
This invention also relates to the use of tocotrienols, tocotrienol-like compounds, and mixtures thereof, as hypocholesterolemic, antithrombotic, antioxidizing, antiatherogenic, antiinflammatory and immunoregulatory agents, or as agents useful to decrease lipoprotein (a) concentration in the blood or to increase feed conversion efficiency.

AN      97:1493      USPATFULL  
TI      Tocotrienols and tocotrienol-like compounds and methods for their use  
IN      Lane, Ronald H., Phoenix, AZ, United States  
Qureshi, Asaf A., Madison, WI, United States  
Salser, Winston A., Pacific Palisades, CA, United States  
PA      Lipogenics, Inc., Scottsdale, AZ, United States (U.S. corporation)  
PI      US 5591772      19970107      <--  
WO 9309777      19930527      <--  
AI      US 1994-244215      19940815 (8)  
WO 1992-US10277      19921120  
19940815      PCT 371 date  
19940815      PCT 102(e) date

RLI      Continuation-in-part of Ser. No. US 1991-796486, filed on 22 Nov 1991, now abandoned

DT      Utility  
FS      Granted

EXNAM      Primary Examiner: Raymond, Richard L.

LREP      Lyon & Lyon

CLMN      Number of Claims: 39

ECL      Exemplary Claim: 1,2,3

DRWN      14 Drawing Figure(s); 13 Drawing Page(s)

LN.CNT 3224

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PI US 5591772 19970107 <--  
 WO 9309777 19930527 <--

SUMM . . . ("T"). Tocotrienols and tocopherols occur naturally in small quantities in a wide variety of plant sources, such as rice bran, **palm oil** and barley (A. A. Qureshi et al., "Lowering of Serum Cholesterol in Hypercholesterolemic Humans by Tocotrienols (Palmvitee)", Am. J. Clin. . . .

SUMM . . . al. (1986), Supra. Various human and animal studies have confirmed the impact of pure tocotrienols, isolated from barley, oats and **palm oil**, on cholesterol biosynthesis, specifically LDL-cholesterol (A. A. Qureshi et al., "Dietary Tocotrienols Reduce Concentrations of Plasma Cholesterol, Apolipoprotein B, Thromboxane. . . Humans By Tocotrienols (Palmvitee)", Am. J. Clin. Nutro, 53, pp. 1021S-26S (1991); D.T.S. Tan et al , "The Effect Of **Palm Oil** Vitamin E Concentrate On The Serum And Lipoprotein Lipids In Humans", Am. J. Clin. Nutr., 53, pp. 1027S-30S (1991)). In. . .

DETD TRF Standard--A tocotrienol-rich fraction (TRF) obtained from **palm oil** (A. A. Qureshi et al. (1991), supra). The TRF Standard contains varying amounts of .alpha.-, .gamma.- and .delta.-tocotrienol and .alpha.-tocopherol. . .

DETD . . . milkweed, flax, sesame, rice bran, parboiled brown rice, brown rice flour, olives, vegetable oil distillant, fruit concentrate evaporate, barley bran, **palm oil**, wheat germ oil, rice bran oil, barley oil, **coconut oil**, **cottonseed oil**, **soybean oil**, other cereal grains and other cereal grain oils, plant tissues, flowers, bushes (such as juniper), trees (such as pine and. . .

DETD Pharmaceutical compositions may take the form of tablets, capsules, **emulsions**, suspensions and powders for oral administration, sterile solutions or **emulsions** for parenteral administration, sterile solutions for intravenous administration and gels, lotions and cremes for topical application. The pharmaceutical compositions may. . .

DETD . . . thereof, and a pharmaceutically acceptable carrier. Such carriers may be solid or liquid, such as, for example, cornstarch, lactose, sucrose, **olive oil** or **sesame oil**. If a solid carrier is used, the dosage forms may be tablets, capsules or lozenges. Liquid dosage forms include soft. . .

DETD . . . used in combination with bile acid sequestrants, such as Cholestyramine and Colestipol; fibric acid derivatives, such as, Clofibrate, Gemfibrozil, Bezafibrate, **Fenofibrate**, and Ciprofibrate; HMGCoA inhibitors, such as Lovastatin, Mevastatin, Pravastatin, Simvastatin and SRI-62320; Probucol; Nicotinic Acid; its derivatives and conjugates, such. . .

Ingredients	Weight (g)
Corn (8.8% protein)	
	615.0
Soybean Meal	335.0
<b>Corn Oil</b>	10.0
Calcium Carbonate	10.0
Dicalcium Phosphate	20.0
Iodized Salt	5.0
Mineral Mixture.sup.a	

2.5  
Vitamin Mixture.sup.b  
2.5

.sup.1 Mineral mixture contained per kg feed: zinc sulfate.H.sub.2. . .  
DETD . . . of the chicken mash diet containing a 5% supplement of various  
oils. The control diet included a supplement of 5% **corn**  
**oil**. After 4 weeks, the birds were fasted for 36 hours and then  
refed for 48 hours prior to sacrifice (at. . .  
DETD . . . Glucose

1)

Chick Diet + 5.0%  
185.1 .+- . 1.5.sup.A  
110.3 .+- . 4.95.sup.A  
61.9 .+- . 4.49.sup.A  
90.2 .+- . 2.17.sup.A  
124.6 .+- . 2.30.sup.A  
  
Corn Oil (CDC)  
(100.0).sup.2  
(110.0).sup.2  
(100.0).sup.2  
(100.0).sup.2  
(100.0).sup.2

2)

Chick Diet + 5.0%  
129.7 .+- . 4.1.sup.B  
99.8 .+- . 3.57.sup.A  
27.9 .+- . 2.60.sup.B  
84.5. . .  
DETD . . . (nmoles/mg/min).sup.3

1)

Chick Diet + 5.0%  
185.1 .+- . 4.12.sup.A  
110.3 .+- . 4.95.sup.A  
61.9 .+- . 1.49.sup.A  
344.3 .+- . 1.49.sup.A  
0.855 .+- . 0.084.sup.A  
  
Corn Oil (CDCO)  
(100.0).sup.4  
(100.0).sup.4  
(100.0).sup.4  
(100.0).sup.4  
(100.0).sup.4

2)

Chick Diet + 5.0%  
184.7 .+- . 6.50.sup.A  
109.6 .+- . 2.83.sup.A  
61.7 .+- . 1.71.sup.A  
339.3 .+- . 19.7.sup.A  
0.837 .+- . 0.081.sup.A  
  
Corn Oil + Waxes;  
(99.8) (99.4) (99.7) (98.5) (97.9)

50 ppm

3)

Chick Diet + 5.0%  
173.8 .+- . 7.31.sup.A  
106.2 .+- . 4.69.sup.A  
58.1 .+- . 1.77.sup.A

317.1  $\pm$  14.4.sup.A,B  
0.846  $\pm$  0.072.sup.A

**Corn Oil + Waxes;**  
(93.9) (96.3) (93.9) (92.1) (98.9)

5,000 ppm

4) Chick Diet + 5.0%  
165.9  $\pm$  4.90.sup.B  
108.5  $\pm$  4.68.sup.A  
57.9  $\pm$  1.48.sup.A  
304.5  $\pm$  14.4.sup.B  
0.902  $\pm$  0.080.sup.A

**Corn Oil + Waxes;**  
(89.6) (98.4) (93.5) (88.4) (105.5)

10,000 ppm

5) Chick Diet + 5.0%  
134.8  $\pm$  3.82.sup.C  
104.3  $\pm$  3.99.sup.A  
25.9  $\pm$  1.02.sup.B  
276.0  $\pm$  17.4.sup.C  
1.068  $\pm$  0.047.sup.B

**Corn Oil + (72.8) (94.6) (41.8) (80.2) (124.9)**  
Tocotrienol-Rich-  
Fraction; 50 ppm

6) Chick Diet + 5.0%  
180.2  $\pm$  6.01.sup.A  
104.0  $\pm$  4.57.sup.A

DETD . . . (ng/ml)

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1) Chick Diet + 5.0%  
61.4  $\pm$  2.4.sup.A  
90.2  $\pm$  1.17.sup.A  
124.6  $\pm$  2.3.sup.A  
16.7  $\pm$  1.69.sup.A  
7.2  $\pm$  0.48.sup.A

**Corn Oil (CDCO)**  
(100.0).sup.3  
(100.0).sup.3  
(100.0).sup.3  
(100.0).sup.3  
(100.0).sup.3

2) Chick Diet + 5.0%  
62.5  $\pm$  1.9.sup.A  
91.5  $\pm$  1.48.sup.A  
126.7  $\pm$  2.1.sup.A  
15.8  $\pm$  1.29.sup.A  
7.5  $\pm$  0.42.sup.A

**Corn Oil + Waxes;**  
(102.0).sup.3  
(101.4).sup.3  
(101.7).sup.3  
(94.6).sup.3  
(104.2).sup.3

50 ppm

3)



Chick Diet + 5.0%

63.6  $\pm$  2.8.sup.B  
95.2  $\pm$  1.01.sup.A  
123.9  $\pm$  1.52.sup.A  
16.4  $\pm$  1.66.sup.A  
7.4  $\pm$  0.36.sup.A

Corn Oil + Waxes;

(103.8).sup.3  
(105.5).sup.3  
(99.4).sup.3  
(98.2).sup.3  
(102.8).sup.3

5,000 ppm

4)

Chick Diet + 5.0%

60.4  $\pm$  1.9.sup.A  
96.1  $\pm$  1.90.sup.A  
124.3  $\pm$  1.18.sup.A  
16.8  $\pm$  1.67.sup.A  
7.4  $\pm$  0.87.sup.A

Corn Oil + Waxes;

(98.5).sup.3  
(106.5).sup.3  
(99.8).sup.3  
(100.6).sup.3  
(102.8).sup.3

10,000 ppm

5)

Chick Diet + 5.0%

68.5  $\pm$  2.1.sup.B  
73.2  $\pm$  1.69.sup.B  
86.4  $\pm$  1.55.sup.B  
12.4  $\pm$  1.42.sup.B  
5.7  $\pm$  0.64.sup.B

Corn Oil + (111.7).sup.3

(81.2).sup.3  
(69.3).sup.3  
(74.3).sup.3  
(79.2).sup.3

Tocotrienol-Rich-  
Fraction; 50 ppm

6)

Chick Diet + 5.0%

65.8  $\pm$  1.2.sup.B  
89.5  $\pm$  1.21.sup.A

. . .